

its origin in absorption of toxin from the digestive apparatus, and it is now recognized by many authorities as a direct cause of this painful and troublesome affection. The state of the skin in these chronic toxic cases is often peculiarly dry and harsh. Affections such as some forms of eczema, psoriasis, and chronic urticaria may arise from a similar cause. I have seen success follow treatment of the colon in obstinate conditions of herpes and dermatitis herpetiformis and also of septic state of the nails.

As to treatment: Diet is of the greatest importance, and must be suited to the peculiar needs of the individual. Speaking broadly, it would appear necessary to consider it as much from a mechanical as from a chemical standpoint. Foodstuffs calculated to leave a residue of undigested particles are apt to set up further colon irritability, and in the many cases where a tendency to spasm exists this can be a source of further trouble. Food must be masticated thoroughly, and eaten slowly. Meals should be "dry" and large quantities of fluid taken between meals.

In conclusion, I would most strongly urge the utmost importance of routine, thorough examination of the abdomen in all cases where there can be a possible doubt as to the origin of symptoms however remotely removed from that region. Too often such a thing begins and ends with an inquiry as to the state of the bowels. In cases where there can still be a doubt, and these are frequently enough met with, lavage of the colon may clear up a diagnosis. In regard to intestinal irrigations, my own experience has been almost wholly confined to those in which the Harrogate sulphur waters have been used as an irrigant, but in some instances where this was not available I have recommended normal saline solution. The fluid employed must be bland in type, and of proper temperature and pressure. The use of antiseptic solutions as a method of treatment is to be deprecated, as their prolonged administration is frequently attended by disastrous results owing to their tendency to produce further irritation.

Mr. FRANCIS BROOK: Neurasthenia has long been suspected to be due in a majority of cases to a toxic condition of the blood originating in an alimentary toxæmia, but hitherto no definite proof of that theory has been brought forward. I venture to think that, on considering the evidence I am about to put before you, you will agree that this theory is no longer mere conjecture, but rests on solid fact. I base this statement on three grounds: Firstly, the clinical symptoms;

secondly, the bacteriological evidence; thirdly, the successful results obtained from treatment on these lines.

Clinically, what are the symptoms of a chronic toxæmia other than alimentary—for example, chronic alcoholism? Are they not prostration, restlessness, headache, irritability, nervousness, disturbed sleep, hyperæsthesia and pains, irritable temper, easy fatiguability, loss of concentration, and loss of memory: and do not these symptoms correspond exactly with the symptoms of neurasthenia?

We now come to the bacteriological evidence. For a long period it has been my practice to examine bacteriologically the fæces in every case of neurasthenia which has come under my care. At Liverpool, last year, at the annual meeting of the British Medical Association, I gave the details of fifty-four consecutive cases of neurasthenia.¹ Every one of these showed an abnormal condition of the flora. At the present time my cases number 132, and I can only say that each successive case confirms me in my belief that chronic intestinal toxæmia is at the root of almost every case of neurasthenic trouble. In considering the bacteriological evidence the first thing to do is, I think, to define what one means by normal intestinal flora, and I would here state that the anaerobes have not been dealt with, and that the medium employed was nutrose-lactose agar with litmus as an indicator. The usual bacteriological picture presented by a culture plate of the above medium, sown with an emulsion of fæces from an average normal healthy individual, shows about 90 per cent. of a mixture of *Bacillus coli communis* and *Bacillus coli communior* in about equal numbers, together with about 10 per cent. of a saprophytic *Streptococcus brevis*.

One hundred and thirty-two cases of neurasthenia in all were investigated, and the bacterioscopic examination gave the following results: *Bacillus coli*, twenty-seven cases; *Streptococcus pyogenes longus* in practically pure culture, sixty-two cases. Here I have not recognized the multitudinous varieties of streptococcus differentiated by some observers upon minor differences of biological characters, and which are undoubtedly due to variations of environmental conditions, but have adhered to the original classification of Lingelsheim into the pathogenic *Streptococcus pyogenes longus*, and the saprophytic *Streptococcus brevis*. *Bacillus coli* associated with *Streptococcus pyogenes longus*, four cases; *Coliform bacilli* in practically pure culture, twenty-five cases. This coliform bacillus (probably an atypical strain of *Bacillus coli*), which produces blue colonies on nutrose-agar plates,

¹ *Brit. Med. Journ.*, 1912, ii, p. 964.

and only ferments the monosaccharides, has been recognized by Distaso and Eyre as causally associated with mucomembranous colitis; indeed, the former observer regards it as practically specific in this connexion. At least two varieties of it may be present, a discrete and a spreading type. *Coliform bacilli* associated with *Streptococcus pyogenes longus*, seven cases; *Bacillus lactis aërogenes* in more or less pure culture, seven cases. Serological observations (agglutination reaction and opsonin estimation) were made in all the cases, except some of the streptococcal ones, and formed a most valuable guide, especially in those cases where the infection was a mixed one. It is interesting to note that of five cases on the lunacy border line, not one showed any change at all from the normal. A point of much interest is that in a large number of the streptococcal cases pyorrhœa was either present or, if not present, a definite history of it could be obtained. And here I think it cannot be too strongly emphasized that the pyorrhœa is the cause and not the result of the intestinal trouble, as some writers appear to infer—the same *Streptococcus pyogenes longus* being isolated in these cases from the pyorrhœa and from the fæces. Another point of interest is that the majority of the coli cases were in women in the neighbourhood of the menopause.

I think it will be agreed that the above analysis also throws much light on the well-recognized connexion of neurasthenia with colitis, a fact which has long been admitted, and also with various forms of chronic arthritis and neuritis. A further point worth recording is that, acting on Schrenk-Notzing's dictum that impotence may be the only symptom of neurasthenia, two cases whose fæces were examined showed very definite infection by streptococcus. One of these patients is quite cured, is now married, and leading a normal sexual life.

Upon the bacteriological results my cases may be classified as follows:—

Class I.—Those in which the bacteriological flora appeared normal as far as could be judged by the cultivations obtained upon nutrient media, and where subsequent investigation by serological methods was needed in order to select such strains of *Bacillus coli* as had undoubtedly acquired pathogenic properties towards their host.

Class II.—Those in which the *Bacillus coli* normally present had partially or wholly disappeared from the intestinal flora, and was replaced by (a) *Streptococcus pyogenes longus*; (b) *Coliform bacillus*; (c) *Bacillus lactis aërogenes*.

[I should here like to record my thanks to Dr. Eyre for the work he has done, and the advice he has given me in making the bacteriological investigations.]

We now come to the treatment and its results. Autogenous vaccines were given in all cases. The dose was always made small at the beginning, and so any constitutional reaction was avoided. Injections were given as a rule once a week, although sometimes at 5-day intervals. Sour milk was given to certain cases, especially those whose fæces were alkaline immediately on evacuation, and I may here say that patients usually feel better when the motions are acid, and not so well when they are alkaline. I have recently employed a preparation of *Bacillus glycobacter* for this purpose, and have found it useful. Intestinal antiseptics were given from time to time, but, except perhaps beta-naphthol and sulphur, I cannot say that I found them of much service. High colon lavage was sometimes prescribed twice weekly, and was certainly of benefit to some cases. Diet did, I think, make some difference to the results. The adoption of a vegetarian diet certainly assisted in rendering alkaline stools acid. Successful results were obtained in the majority of the cases, and in many where previous treatment by other methods had completely failed. The improvement, both physical and mental, always coincided with the disappearance of the abnormal flora from the intestinal canal, and those cases which were not cured were those where nothing that one could do caused a return of the normal flora. These cases were almost invariably streptococcal in type. The treatment occupies in most cases about three months, the majority of them getting well in that time. The rapidity of the improvement in some cases is such as to be almost startling. With regard to the permanence of the cure, some of the cases have been under observation over two years, and they remain perfectly well to-day. From the patient's point of view, one of the greatest advantages of this mode of treatment is that it can be quite well carried out at home, and does not necessitate absence from his duties if he is able to work.

In Class I, where the plate cultivations appeared normal, evidence of infection by *Bacillus coli* was obtained in every case by means of serological tests—for example, agglutination reactions and opsonin estimations, and improvement followed upon the use of the appropriate autogenous vaccine. In Class II (a) the *Streptococcus pyogenes longus* was present, and under treatment the improvement manifested clinically, was coincident with the disappearance of the streptococci from the fæces and the reappearance of the typical *Bacillus coli*. In Class II (b) the same remark applies to the clinical improvement as the coliform bacilli disappeared. In Class II (c) (*Bacillus lactis aërogenes*),

two of the cases were seen once only and were not treated; the five which were treated made excellent recoveries.

One of the most striking results was the rapid improvement in the physical appearance; the pallor, muddy complexion, dark circles under the eyes, and blueness of the lips so often present, rapidly gave place to a healthy colour, the eyes became brighter and lost their dull heavy look, and the face lost its appearance of premature age. The indigestion, aching pains, lassitude, and irritability disappeared, and the change in the mental condition was equally marked. The memory and power of concentration improved, the depression and insomnia passed away, and the whole outlook on life became quite changed, and in fact normal, and marked increase in weight often occurred.

Neurasthenia has been classified according to whether the blood-pressure is high, normal, or low. Whether this classification is of any very great importance I do not venture an opinion, but I wish to call attention to the fact that in several cases where the blood-pressure was high it fell steadily during the course of the treatment.

TRAUMATIC NEURASTHENIA.

With regard to traumatic neurasthenia, in a recent address given at Milan by Professor Murri, published in the *Universal Medical Record*,¹ he points out that "cause" only exists as a complex of determining conditions, and that most frequently the accident is but the occasion that reveals pre-existing disorder, or that gives effect to it when the conditions are already ripe. The effects, therefore, are not specific to the occasion, but to the precedent condition. Of the two cases of traumatic neurasthenia I have so far investigated, one showed definite evidence of *Bacillus coli* infection, and the other gave a pure cultivation of *Bacillus lactis aërogenes*.

SUMMARY.

I would summarize my observations by advancing the opinion that the bacteria referred to bore a direct causal relationship to these cases of neurasthenia, for the following reasons:—

(1) An abnormal condition of the intestinal flora was present in more than half the cases.

(2) Serological tests yielded evidence of infection by the abnormal bacteria, and by some of the strains of colon bacilli in each of those cases where the intestinal flora appeared at first to be normal.

¹ *Universal Med. Record*, 1912, ii, pp. 10, 97.

(3) Most important, the improvement in the patient's condition, both physical and mental, under treatment synchronized with the reappearance of the normal intestinal saprophytes in the fæces, and the disappearance of the abnormal organisms.

(4) Of course, one realizes that the personal element and the factor of suggestion cannot be eliminated, yet many of the patients who were cured had previously tried other recognized forms of treatment—rest cures, high frequency, Weir Mitchell hydropathy, &c.—where these same factors were at work; hence I do not think that they can fairly be said to have had much influence on the results.

I will now give you some illustrative cases, dividing them into (a) those which were successful, (b) those which were not; in these latter the intestinal flora remained practically unaltered in spite of the treatment. I may here point out that neither the symptoms complained of nor the clinical appearance of the patient give any indication as to the variety of bacterial infection which will be found on examination of the fæces. The following notes have been taken from my case-book just as they were entered. In choosing these cases for illustration, I have purposely taken those of least recent date as giving a better idea of the permanence of the results.

SUCCESSFUL CASES.

Class I.—Bacillus coli.

Case I.—Mrs. A. C., aged 46, married, no children. Healthy till an attack of influenza three years ago; then anæmia, depression, chronic rheumatic pains, and some neuritis. In spite of treatment, rest cures, various kinds of baths both here and abroad, the condition, with the exception of the neuritis, remained unchanged. She complained of great depression, loss of memory, lack of concentration, irritability, and bad rheumatic pains (the joints appeared normal), and also of the ease with which she became fatigued. Complexion was muddy, and the eyes dull and heavy. The fæces, culturally and microscopically, appeared normal, but *Bacillus coli* gave an opsonic index of 1'5. Treatment commenced July, 1911. After the eighth injection the depression had disappeared. She stated that she felt well and had plenty of energy, and could walk without fatigue. After the twelfth injection the index was 1'09. The will and mind were clear and the memory good. In April, 1913, she reports herself perfectly well, and the opsonic index is 1'2.

Case II.—Mrs. F. C., aged 40, married, no children. History of an attack of what was apparently ptomaine poisoning one year ago, since when she has never been well. Has suffered from a feeling of heaviness in the appendix

region for four years. Complains of inability to walk more than a few yards without intense fatigue. Pains in the limbs, especially in the legs. She is constipated and never has an action without drugs. Acidity, feeling of fullness after meals, palpitation, sleep and appetite good, anæmic, the complexion muddy, skin dry, dark circles under the eyes. Fæces apparently normal; gave an index to *Bacillus coli* of 1.5. Treatment began November, 1911. She said she felt better after the first dose. Improvement was rapid, and after a month she could walk some distance without fatigue. Complexion became normal, and the face much fuller. When seen fifteen months later she was well, and in a recent letter states that she has remained so.

Class II (a).—Streptococcus pyogenes longus.

Case I.—A. S., male, aged 36, married, schoolmaster. Neurasthenia three years, which latterly became so bad that he had to resign his position as headmaster of a public school. The first symptom noticed was a burning feeling of the face, hand, and back of the neck; then followed lassitude, depression, and great irritability. He had no constipation, but was always worrying about the action of the bowels, the stools being always light-coloured. The blood-pressure was 200 mm. The reflexes slightly exaggerated, marked insomnia, frequent micturition, great physical weakness. *Streptococcus longus* was present in pure culture. Treatment commenced March, 1911. After the second injection he walked 20 miles, and was much more cheerful. At the beginning of May the *Bacillus coli* equalled the streptococci in numbers. Head much better. Blood-pressure 170. In July, much better generally, blood-pressure 150, streptococci diminishing, insomnia only causes one bad night in five. In November, no insomnia for three months, no depression, blood-pressure 160. Fæces have resumed normal type, culturally and microscopically. He has taken up cross-country running, and in January, 1913, writes that he is perfectly fit.

Case II.—Mrs. T., aged 37, married, three children, youngest aged 7. Colitis in India seven years ago. Six years' history of neurasthenia. Complained of great lassitude, depression, insomnia, loss of power of concentration, pains in legs, and chronic abdominal dragging pain, previously supposed ovarian in origin, but probably coming from the colon. No constipation, complexion muddy, skin dry, dark circles under the eyes, very anæmic. Fæces showed almost pure cultivation of *Streptococcus longus*. Treatment commenced April, 1911. The symptoms rapidly cleared up, especially the abdominal pain. Sleep and spirits became good, and the complexion normal. In September the fæces were microscopically and culturally normal. In a recent letter she reports that she is in excellent health.

Class II (b).—Coliform bacillus.

Case I.—G. W., aged 45, married, railway manager. Two years ago he suffered with a constant feeling of vertigo; he used to perspire very freely, at

first only at night, then in the day also. Complains of a feeling of dread, and undefined haunting fear of doom. No cause at all. Sleeps very heavily, but always dreaming. Great lassitude. Occipital headache, and burning feeling on the top of the head. Bowels open daily with salines. Twitchings of arm and face; horror of noise; great depression; very easily tired. Has tried several forms of treatment. On cultivation of fæces, coliform colonies appeared, the opsonic index to which was 1'91, while to the normal coli it was 1'0. Treatment commenced in February, and there was rapid improvement from that date. In a fortnight the depression had disappeared, and dreams and fatigues were less. At the end of three months he was well, and now reports that his condition, both physical and mental, remains excellent, and that he enjoys his work, which had previously become a burden to him.

Case II.—W. P., aged 29, an accountant. Was quite well till nine months ago, when the present symptoms became manifest. He complains of worrying greatly about things (the condition becoming rapidly worse), lack of concentration, heavy sleep with bad dreams. He goes over and over his additions, because he thinks there may be an error. Has a dragging feeling on the top of the head, and sensation of swimming in the head when reading or doing any head work. Occasionally, when walking, he feels as though he reels, but does not actually do so. He never feels fit. Fæces showed coliform bacilli, index 1'4. Treatment was commenced in December. The symptoms gradually abated. He was able to add easily without going over the work more than once. The swimming feeling passed away, and in April he reported that he was absolutely well, and just going to get married. The fæces had then resumed normal type.

Class II (c).—Bacillus lactis aërogenes.

Mrs. N. G., aged 60, married, no children. Ten years' history of neurasthenia, in the course of which she had tried many forms of treatment without effect. She complained of a feeling of absolute exhaustion, as though dying, and that to do the slightest thing was a "mountainous" effort. Frightful depression. Very highly strung, keeps going till she drops. Flatulence, acidity after every meal, pain and tenderness over colon on right side. Sleep broken by bad dreams; constant ringing in ears. Head always feels too heavy, and as if falling backwards. Mucus in stools, which are usually constipated. The patient was very anæmic, complexion pasty and yellow, skin dry, sclerotics yellow; blood-pressure 240, pulse 56. *Bacillus lactis aërogenes* in pure culture in the fæces. Treatment was followed by rapid improvement, digestion became good, the depression disappeared, and also the abnormal feeling of fatigue. Complexion cleared, and after ten injections the patient was quite well. The blood-pressure in the meantime had fallen to 170, and the pulse had risen to 68. After twelve months she has remained quite well.

We now come to the unsuccessful cases. These were quite small numerically, and usually streptococcal. They were not absolute failures, but they were not cures.

UNSUCCESSFUL CASES.

Case I.—E. E., aged 46, musician. Ill eight years. When he entered my consulting-room he announced that I was the twenty-eighth doctor by whom he had been treated. Operation on left kidney eight years ago for supposed renal colic. Nothing was found, and I have no doubt the pain had its origin in the colon. Twenty-eight weeks in bed last year. Complains of great lassitude, weakness, irritability, and depression. Every molehill appears a mountain. Periodical attacks of pain, very acute in left side of abdomen, running down to legs. Diarrhœa and unformed stools. Fæces showed streptococci in nearly pure culture. Treatment commenced February, 1911. He improved steadily in spirits, energy, and colour, which had been very pasty. In May the streptococci equalled the *Bacilli coli* in number. Stools now formed. In November, after a lapse of three months, the streptococcus to coli ratio was back to 10 to 1. In February the numbers were equal, and there he remains for the present. Twelve months later he reports his condition slowly improving. He is immensely better and looks a different man, and he has only had one day away from work in eighteen months, but I cannot say he is cured. I have discussed removal of his colon with him, but this he has refused.

Case II.—G. D. C., aged 49, male. Ill six months. Complained of vertigo and a feeling of reeling, although he never did so. Depression, lassitude, pains in legs, irritability. Sclerotics yellow, skin dry, eczema of old standing. Blood-pressure 180. Fæces showed streptococci in almost pure culture. Treatment begun in July, 1911. Gradual improvement took place in his condition, and in October the streptococci and coli were in equal numbers; blood-pressure 130. In January, although his condition remained about the same, the culture showed nearly all streptococci again. In February they were again equal; blood-pressure 126. He was much better, but not well, and then went to Switzerland. This case was one of those in which I tried a vegetarian diet for a time, but gave it up as it did not seem to be benefiting the patient.

DR. WILLIAM ARMSTRONG: I should like to record the results of sixteen years' study of the many problems of alimentary toxæmia, and the lessons I have learnt regarding its treatment. Since I first wrote on this subject some fifteen years ago, great strides have been made in the scientific study of the intestinal ferments and flora, and their behaviour. But I doubt if similar progress can be claimed for the therapy.